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Stabilization of Dyes Against Hydrolytic Decomposition by the Formation of Inclusion Compounds

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Abstract. The decomposition reactions of the dyes phenol blue and murexide were measured spectroscopically in acidic solution at different temperatures. From these reaction rates and their temperature dependence in the absence and presence of various hosts, the stability constants and the reaction enthalpies of the dye complexes with noncyclic dextrins, cyclodextrins and cucurbituril were calculated. β-Cyclodextrin enhances the stability of phenol blue in acidic solution. This effect is even more pronounced with cucurbituril. Due to the molecular structure of murexide this dye cannot form inclusion complexes with hosts containing hydrophobic cavities.

Key words. Dye complexes, inclusion compounds, cyclodextrins, cucurbituril.

1. Introduction

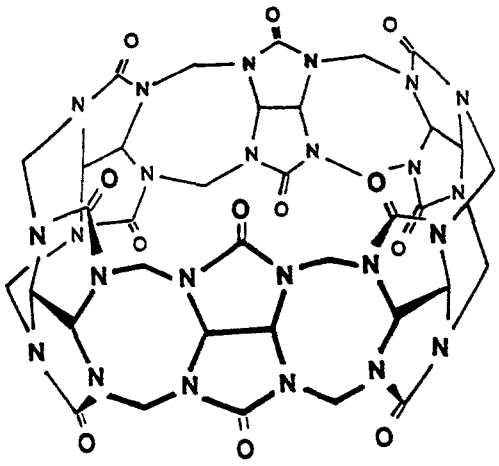
The formation of inclusion compounds generally changes the chemical and/or physical properties of the complexed ions or molecules. As an example, the inclusion of air sensitive substances into cyclodextrins results in their stabilization with respect to oxidation [1]. Many further examples have been noted in the literature [2].

The formation of inclusion complexes with dyes may result in different behaviour of these dyes. Thus, the stabilization of a light sensitive dye due to complexation by cyclodextrins has already been reported [3]. However, dyes which are destroyed in acidic or alkaline solutions may be stabilized in a similar manner. To shield them from the solution, hosts should be used having three-dimensional cavities (e.g. cyclodextrins). The formation of dye complexes with such hosts is well known for cyclodextrins [2, 5] and to our knowledge only with a few other cyclophanes [6–9].

The macrocyclic structure of host (**I**) was not known for a long time until Freeman *et al.* reported its structure [10]. They proposed the trivial name cucurbituril due to the complexity of its systematic name. Both cyclodextrins and cucurbituril are more or less rigid molecules with fixed cavity dimensions. In the case of the cyclodextrins it is known that the cavities are apolar in aqueous solutions [11]. Similar results are found for cucurbituril [12]. The hydrophobicity inside the cavities should favour the inclusion of dyes. These molecules, or parts of them, are normally rather hydrophobic.

2. Experimental

The cyclodextrins (Fluka) were used without further purification. Noncyclic dextrins such as Dextrin 10 (MW = 1100) and Dextrin 20 (MW = 1000) (all Fluka)



I: Cucurbituril.

were also used. The determination of the medium molecular weights of the dextrins has already been reported in the literature [13].

Cucurbituril was synthesized and purified as described in the literature [6, 10]. The ligand was characterized by elemental analysis, by mass spectral analysis and by ^{1}H- and ^{13}C-NMR spectra [14].

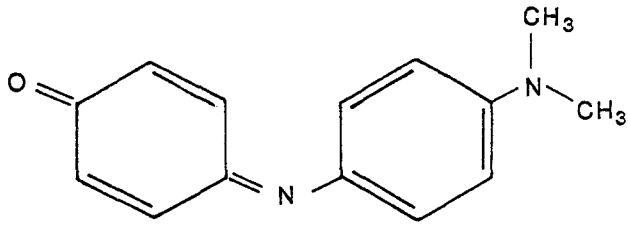
The following dyes were used without further purification: phenolblue (**II**) (Aldrich) and murexide (**III**) (Merck).

All solutions were prepared with doubly distilled water. The dye concentrations were below 1×10^{-4} mol l^{-1}. The concentration of the ligands were always much higher in order to achieve a complete complexation of the dyes. This was tested by a variation of the ligand concentrations which did not result in any change of the rate constant of decomposition. Hydrochloric acid was used to acidify these solutions. No activity corrections were made since the concentration of the protons was rather high in all experiments and all reactions were measured within the same proton concentration range. The results are thus strictly comparable.

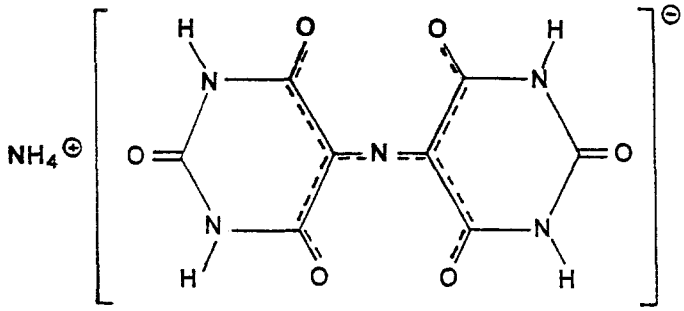
The decomposition of the dyes was observed spectroscopically using a Perkin Elmer 330 spectrophotometer with thermostated cuvettes. The changes of the color with time were recorded at the maximum of the absorption for each dye (phenol blue: 578 nm, murexide: 515 nm). In all cases examined these reactions were first order. The rate constants were calculated using a computer program [15]. The reproducibility of the rate constants was better than 10%.

3. Results and Discussion

In acidic solution phenol blue readily decomposes to *p*-benzoquinone and the corresponding diamine and murexide to uramil and alloxan. The experimentally



II: Phenol blue.



III: Murexide.

measured rate constant of decomposition, k', depends on the proton concentration of the solution. If an uncatalysed decomposition reaction with the rate constant k_0 takes place at the same time then k' is given by the following equation:

$$k' = k_0 + k_H \cdot [H^+].$$

The rate constant for the proton catalysis is k_H.

To find out whether or not the decomposition reaction is influenced by the complexation of the dye these reaction rates are estimated using one proton concentration and one temperature, with and without addition of host. The results for the decomposition of phenol blue in the presence of different hosts are given in Table I. The measured reaction rates clearly demonstrate the interaction of phenol blue with some of the hosts examined. However, from the absence of any effect on the rate of decomposition with the other hosts no conclusion may be drawn about the interactions between these hosts and the dye molecules. It is known that the formation of complexes of noncyclic dextrins with organic guests is possible [16–18].

The rate of decomposition of phenol blue is reduced in the presence of β-cyclodextrin and of cucurbituril. The rate is reduced by a factor of 2 in the presence of β-cyclodextrin and by a factor of 100 in the presence of cucurbituril.

To obtain more information about this stabilization effect the decomposition of phenol blue was measured at different acid concentrations and temperatures. The experimental values of k' in the presence of cucurbituril are shown in Figure 1. From a linear fit of the data one may obtain a value of k_H from the slope and a

Table I. Rate constants k' ($l\,s^{-1}\,mol^{-1}$) for the decomposition of phenol blue at an acid concentration of $c_H = 0.1\ mol\,l^{-1}$ at 25°C

Host	k'
none	3.51×10^{-3}
α-Cyclodextrin	3.43×10^{-3}
β-Cyclodextrin	1.60×10^{-3}
γ-Cyclodextrin	3.53×10^{-3}
Dextrin 10	3.50×10^{-3}
Dextrin 20	3.46×10^{-3}
β-Cyclodextrin + Dextrin 10[a]	1.38×10^{-3}
β-Cyclodextrin + Dextrin 20[a]	1.34×10^{-3}
γ-Cyclodextrin + Dextrin 10[a]	3.72×10^{-3}
Cucurbituril	2.66×10^{-5}

[a] $10\ g\,l^{-1}$ Cyclodextrin and $10\ g\,l^{-1}$ Dextrin.

value of k_0 from the intercept, while the temperature dependence of these quantities can be used to calculate the corresponding activation energies and entropies. The values for the proton catalysed reaction are summarized in Table II and for the uncatalysed reaction in Table III.

To discuss the results the following reaction scheme may be postulated:

$$A \underset{k_2}{\overset{k_1}{\rightleftharpoons}} B \xrightarrow{k_3} C$$

with A as the complexed dye, B as the uncomplexed dye, and C as the colourless decomposition products. The rate constants k_1 and k_2 describe the complex

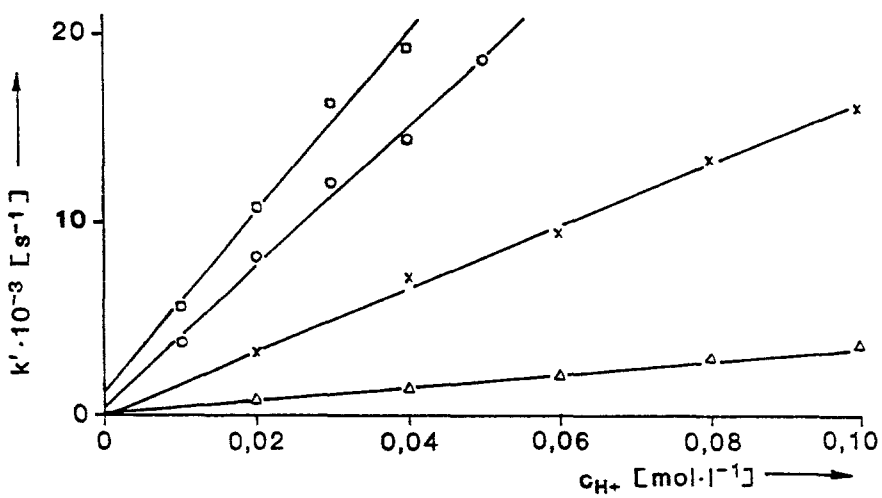


Fig. 1. Rate constant, k', for the decomposition of phenol blue as a function of the proton concentration at different temperatures (△ 25°C, × 50°C, ○ 68°C, □ 78°C).

Table II. Rate constant k_H ($l\,s^{-1}\,mol^{-1}$) for the proton catalysed decomposition of phenol blue, the activation energy $E_A(H)$ ($kJ\,mol^{-1}$) and the entropy of activation $\Delta S(H)$ ($J\,K^{-1}\,mol^{-1}$) at 25°C

Host	k_H	$E_A(H)$	$\Delta S(H)$
none	3.65×10^{-2}	43.7 ± 1.8	-134 ± 6
Dextrin 10	3.65×10^{-2}	48.3 ± 1.1	-119 ± 3
Dextrin 20	3.56×10^{-2}	49.4 ± 1.1	-115 ± 3
β-Cyclodextrin	1.60×10^{-2}	60.8 ± 2.2	-84 ± 7
β-Cyclodextrin +Dextrin 10[a]	1.50×10^{-2}	61.5 ± 1.0	-82 ± 3
β-Cyclodextrin +Dextrin 20[a]	1.51×10^{-2}	61.2 ± 2.9	-83 ± 9
Cucurbituril	3.89×10^{-4}	83.7 ± 4.9	-38 ± 13

[a] $10\,g\,l^{-1}$ β-Cyclodextrin and $10\,g\,l^{-1}$ Dextrin.

Table III. Rate constant k_0 (s^{-1}) for the uncatalysed decomposition of phenol blue, the activation energy E_A ($kJ\,mol^{-1}$) and the entropy of activation ΔS ($J\,K^{-1}\,mol^{-1}$) at 25°C

Host	k_0	E_A	ΔS
none	1.38×10^{-5}	76 ± 6	-93 ± 17
Dextrin 10	–[a]		
Dextrin 20	–[a]		
β-Cyclodextrin	–[a]		
Cucurbituril	4.94×10^{-5}	125 ± 19	83 ± 60

[a] Negative values.

dissociation and formation and k_3 the decomposition of the free dye. At high ligand concentrations the concentration of the free dye in solution is very small. If the equilibrium between A and B is established very quickly, then the observed rate constant k' is given by the following equation

$$k' = k_3 \cdot 1/(1 + K)$$

with $K = k_2/k_1$ as the equilibrium constant (see Appendix).

Because the rates of formation and dissociation of complexes between dyes and α-cyclodextrin are very fast [19] the assumptions made should be valid.

The rate constant k_3 is available from separate experiments for the decomposition of the dye in the absence of any host. Therefore the stability constants for the complexation of this dye by different ligands can be calculated. From the temperature dependence of the decomposition reaction of phenol blue in the absence of any host one can obtain the activation energy E_A of this reaction. As can be seen from the equation given above for k', the activation energy E'_A of k' also depends on the reaction enthalpy for the equilibrium, ΔH, and E_A. It is thus possible to calculate the stability constants and reaction enthalpies for the complexation of phenol blue by the different hosts from the data summarized in Table II. The tabulated results

for k_H and $E_A(H)$ can be interpreted as k_3 and E_A if no host is present, and as k' and E'_A in all other cases. The calculated stability constants and thermodynamic data are given in Table IV.

The noncyclic dextrins form rather weak complexes with phenol blue [20]. Comparable results are known for other dyes [17, 18]. These hosts can wrap around the dye molecule and surround it. No specific interactions take place. With a preformed cavity in the host molecule the nonpolar dye molecule can establish stronger interactions with the host molecule. On the other hand this preorganisation causes less favourable changes of the reaction entropy compared with the flexible noncyclic dextrins because the nonlinear dye molecule has to adapt to the cavity of β-cyclodextrin.

Mixtures of cyclodextrins and the noncyclic dextrins give the same results as obtained with the pure cyclodextrins. No further stabilization of phenol blue takes place, as can be seen from the kinetic and thermodynamic parameters. No simultaneous complexation of the dye by noncyclic and cyclic dextrins is observed.

The cavity of cucurbituril is even more rigid than that of β-cyclodextrin. Therefore the value of the reaction entropy increases even further. Due to more favourable enthalpic changes the stability of this complex is the highest. With phenol blue cucurbituril forms the most stable complex of the hosts examined. As a result the decomposition of the dye is very slow.

The half-life of phenol blue in acidic solution (0.1 mol l^{-1}) at 25°C can easily be calculated using the reaction rates given in Table I. In the absence of any host half of the dye is destroyed after 3.3 min, in the presence of β-cyclodextrin after 7.2 min, and in the presence of cucurbituril only after 434 min.

The reaction rates, k_0, for the nonproton catalysed decomposition (see Table III) are obtained by an extrapolation to zero proton concentration for every host. As a result these constants have a higher uncertainty than the other values of reaction rates. No general trends can be obtained from the estimated reaction rates k_0.

It is known that the protonated form of murexide is also unstable [21]. The decomposition of this dye in acidic solution was also measured at one acid

Table IV. Stability constants K (mol l^{-1}) and reaction enthalpies ΔH (kJ mol^{-1}) and entropies ΔS (J K^{-1} mol^{-1}) for the complexation of phenol blue by different hosts in water at 25°C

Host	K	$-\Delta H$	ΔS
Dextrin 10	≈0	4.6 ± 2.9	
Dextrin 20	3×10^{-2}	5.7 ± 2.9	−48 ± 9
β-Cyclodextrin	1.3	17.1 ± 4.0	−55 ± 14
β-Cyclodextrin + Dextrin 10[a]	1.4	17.8 ± 2.8	−57 ± 9
β-Cyclodextrin + Dextrin 20[a]	1.4	17.5 ± 4.7	−56 ± 16
Cucurbituril	92.8	40.0 ± 6.7	−97 ± 22

[a] 10 g l^{-1} β-Cyclodextrin and 10 g l^{-1} Dextrin.

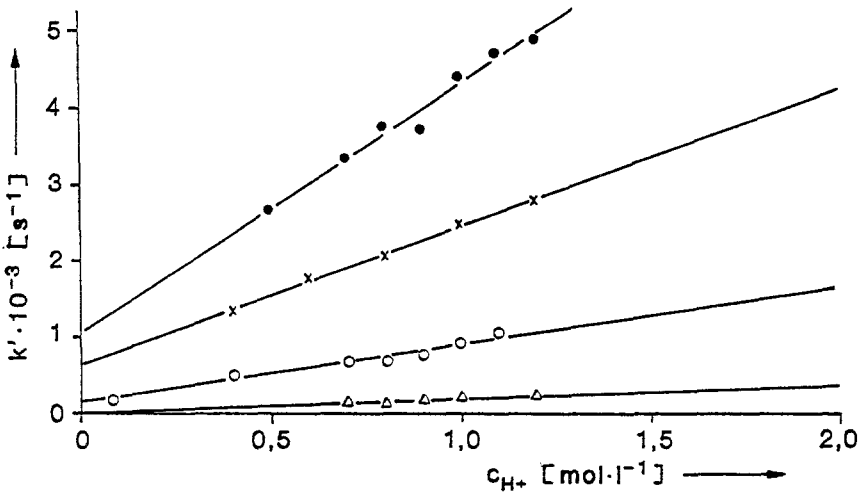


Fig. 2. Rate constant, k', for the decomposition of phenol blue in the presence of cucurbituril as a function of the proton concentration at different temperatures (△ 25°C, ○ 32°C, × 40°C, ● 45°C).

concentration. The observed rate constants for a given proton concentration with and without any host are summarized in Table V. No increase in the stability of this dye molecule is observed with different hosts. Obviously no interactions between the dye and the host molecules take place.

The different behaviour found for phenol blue and murexide can only be explained by the differences in the molecular structure of both dyes. Both dyes have rather similar molecular dimensions. In the middle of the murexide molecule four highly charged oxygen atoms are located. As a result no real hydrophobic parts of this dye molecule exist. The formation of inclusion complexes of murexide with hosts containing a hydrophobic cavity is therefore improbable.

Table V. Rate constants k' ($l\,s^{-1}\,mol^{-1}$) for the proton catalysed decomposition of murexide at an acid concentration of $c_H = 5 \times 10^{-3}$ mol l^{-1} at 25°C

Host	k'
none	4.99×10^{-3}
Dextrin 20	4.84×10^{-3}
β-Cyclodextrin	5.11×10^{-3}
γ-Cyclodextrin	5.47×10^{-3}

Appendix

For the reaction scheme

$$A \underset{k_2}{\overset{k_1}{\rightleftharpoons}} B \xrightarrow{k_3} C$$

one can assume that the reactions forming A or B are fast compared with the formation of C. Under these conditions the actual concentrations of all species may be expressed as the sum of the equilibrium concentrations and a variable x. For example the actual concentration of the species A [A] is given by the following equation

$$[A] = [\bar{A}] + x_A. \tag{1}$$

For the equilibrium between the substances A and B the equilibrium constant is defined by

$$K = k_2/k_1 = [A]/[B] = [\bar{A}]/[\bar{B}] \tag{2}$$

and using the equilibrium concentrations and the variables x one obtains

$$K = \frac{[\bar{A}] + x_A}{[\bar{B}] + x_B} = \frac{[\bar{A}]}{[\bar{B}]} \tag{3}$$

or

$$x_A = \frac{[\bar{A}]}{[\bar{B}]} \cdot x_B. \tag{4}$$

The total concentration of all species c_t is:

$$c_t = [A] + [B] + [C] = [\bar{A}] + x_A + [\bar{B}] + x_B + [\bar{C}] + x_C, \tag{5}$$

where the sum of all the xs is zero:

$$x_A + x_B + x_C = 0. \tag{6}$$

Combination of Equations (4) and (6) leads to

$$x_B \cdot (1 + K) = -x_C. \tag{7}$$

The change in the concentration of the substance C with time may be expressed in the following way:

$$\frac{d[C]}{dt} = k_3 \cdot [B] \tag{8}$$

or

$$\frac{d[\bar{C}]}{dt} + \frac{dx_C}{dt} = k_3 \cdot [\bar{B}] + k_3 \cdot x_B. \tag{9}$$

The equilibrium concentration of C does not change with time and the term $k_3 \cdot [\bar{B}]$ is nearly zero because the formation of C is irreversible, so Equation (9) can be simplified to give:

$$\frac{dx_C}{dt} = k_3 \cdot x_B. \tag{10}$$

Using Equation (7), Equation (10) can be rewritten as

$$\frac{dx_C}{dt} = -k_3 \cdot \frac{1}{1+K} \cdot x_C. \tag{11}$$

The experimentally observed concentration change is described by

$$\frac{dx_C}{dt} = -k' \cdot x_C. \tag{12}$$

Thus, comparing Equations (11) and (12) one obtains:

$$k' = k_3 \cdot \frac{1}{1+K}. \tag{13}$$

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